Mathematical modelling of ion channels

Further Particulars

1. The appointment

We invite applications for a Postdoctoral research position, funded by the King Abdullah University of Science and Technology (KAUST) Global Research Partnership (GRP), to work with Prof. S.J. Chapman and Dr R. Erban at the newly established Oxford Centre for Collaborative Applied Mathematics (OCCAM). This position is available from 1 April 2009.

2. Background

OCCAM has been established with substantial funding from the KAUST GRP. The Centre, which is part of the Mathematical Institute, is allied to a global network of mathematicians. Aiming to meet the ever-increasing global demand for quantitative understanding of complex scientific phenomena, OCCAM has been built on the strength of four pre-existing groups of applied and computational mathematicians working in Oxford: the Oxford Centre for Industrial and Applied Mathematics, the Centre for Mathematical Biology, the Numerical Analysis Group and the Computational Biology Group. It has a symbiotic relationship with other scientific communities which have a need for problem-solving mathematics both within the University of Oxford and beyond. Over the first five years the centre will employ 40 new staff and students.

3. Project

Ion channels and ion pores are proteins situated in cell membranes. They provide a path for rapid movement of ions and water, connecting the cell interior to its exterior through the hydrophobic barrier of the membrane. Channels and pores can be ion selective, allowing only specific ions to permeate through them (for example potassium, sodium, calcium or chloride ions), or non-specific, permeable to a variety of ions. In addition, many channels and pores can change their conformation between open and closed states spontaneously, or in response to stimuli such as a potential difference across the membrane or interaction with various molecules (neurotransmitters, second-messenger drugs). These features are the key to their importance, since they enable control of the interior environment of the cell. Indeed, ion channels are responsible for a vast range of biological function in health and disease. As a result there is huge interest in understanding and manipulating their behaviour. The characterisation of this behaviour, and of the alterations that occur due to mutations (hereditary disease), or as a result of channel blocking drugs, is central to the development of strategies for targeted therapies. Such understanding will also facilitate the construction of synthetic ion channels that can act as highly accurate biosensors.

The modelling approaches that have previously been adopted to describe ion channels include (in ascending order of lengthscale and descending order of complexity) Brownian dynamics (Langevin equations), Fokker-Planck equations, the Poisson-Nernst-Planck (PNP) model and the Eyring Model. In Brownian dynamics the stochastic Langevin equations are used to treat individual ions and Poisson's equation is used to calculate the electric field as a function of the positions of the ions (water molecules are considered as a continuous background). The associated Fokker-Planck equation provides the probability of finding ions at particular positions. The PNP model is a continuum model, formulated in terms of advection-diffusion equations, for ion concentration (or equivalently probability density) and can be derived from the Fokker-Planck equations under a closure assumption. On an even coarser scale the channel is frequently modelled by the stochastic Eyring model; this gives the probabilities of ions jumping between various energy wells within the channel, as a function of the energy required to surmount the intervening energy barriers. Crucially
this energy landscape is modulated by the potential difference across the membrane so that the probability flux of an ion species across the channel depends on the potential drop across it.

Each of the models has its champions, but as yet there has been little work examining the relationship between them. The goal of this project is to examine systematically the relationship between the different models and thereby understand mathematically the limitations of the simpler models (which are computationally feasible) in order to improve them systematically, rather than through ad hoc fudge factors.

The project will involve interaction with both Prof Hagan Bayley’s group in Chemistry and Prof Mark Sansom’s group in Biochemistry. Predictions from the models will be compared with real data for particular ion channels, focussing on one pore (Alpha-hemolysin pore, both wild type and mutants) and one channel (Potassium channel K_{CXA}, about which much is known, and on which Prof Bayley's group is currently working). Although data fitting methods have been used elsewhere we are interested in understanding the errors contained in the model when used without fudge factors so that we can properly evaluate any improved models.

4. Core Groups

4a. Oxford Centre for Industrial and Applied Mathematics
The Oxford Centre for Industrial and Applied Mathematics (OCIAM), part of the Mathematical Institute at Oxford University, contains 14 permanent faculty, 11 postdoctoral researchers, and 25 D.Phil. students. In addition, a number of key players from The Smith Institute Knowledge Transfer Network in Industrial Mathematics are all based in OCIAM. The aim of the group is to develop relationships between mathematicians and industry and other academic departments leading to high quality research with a practical basis. Research in the Centre includes basic science along with a wide range of applications including industrial topics, environmental and medical applications. Regular interdisciplinary workshops are held and there is a weekly seminar on Differential Equations and Applications. Further details can be found at www.maths.ox.ac.uk/ociam

4b. Numerical Analysis Group
The Numerical Analysis Group is a leading centre of expertise in the field of Computational Mathematics. It is part of the Computing Laboratory at Oxford University, and includes 7 permanent faculty, 4 postdoctoral researchers and 12 doctoral students. The group is active in research across most of the areas of numerical analysis and scientific computing, and has strong links with Oxford engineering and mathematics groups and with academic and industrial partners around the UK and abroad. The group runs a regular research seminar series in Computational Mathematics and Applications. Further details are available from: http://web.comlab.ox.ac.uk/oucl/research/na/

4c. Centre for Mathematical Biology
The Centre for Mathematical Biology (CMB), part of the Mathematical Institute, is designed specifically to foster interdisciplinary research in the area. The CMB embodies mathematicians, physical and life scientists, emphasising lively multidisciplinary team work with other research groups within the university, the UK and abroad. The CMB comprises 3 permanent faculty, 1 research fellow, 5 postdoctoral researchers and 16 doctoral students. The group’s research encompasses areas as diverse as modelling social insect behaviour, tumour dynamics, wound healing, pattern formation and signalling in developmental biology, bacterial chemotaxis, regional dynamics of plants, medical imaging, gene-delivery, imaging and mechanics of sperm dynamics and muco-ciliary dynamics. Further details can be found at http://www2.maths.ox.ac.uk/cmb/index.html

4d. Computational Biology Group
The interests of the Computational Biology Group (CBG) within the Computing Laboratory focus on the mathematical modelling, numerical analysis, software engineering and (parallel) scientific programming research issues arising in the multiscale solution of non-linear partial differential equations governing physical transport processes and soft tissue modelling in biological and
physiological systems. The group currently consists of 9 permanent faculty, 10 post-doctoral researchers, and 12 doctoral students. The group holds regular seminar series for external and internal speakers. Further details can be found at http://www.comlab.ox.ac.uk/activities/compbio/

The core groups jointly run a highly successful MSc in Mathematical Modelling and Scientific Computing, which currently has 19 students. The CMB and CBG are integrally involved in the Oxford Centre for Integrative Systems Biology, and the Life Sciences Interface and Systems Biology Doctoral Training Centres.

5. Selection Criteria

(Essential criteria) The successful applicant will be expected to have:-

- PhD (awarded or submitted, at the time of taking up the award) in applied mathematics or a related discipline;
- familiarity with partial differential equations;
- experience of scientific computation;
- the ability to pursue research as part of an interdisciplinary team.
- excellent communication skills;
- a good publication record, judged by the stage of career;

In addition the following are desirable selection criteria:-

- expertise in asymptotic analysis;
- familiarity with stochastic differential equations;
- background knowledge in ion channel modelling;
- good organisational skills

Candidates should explain in their covering letter how they satisfy these criteria.

6. Terms and Conditions

Salary: Starting Salary £28,839-£30,594

Hours: Hours of work are such as are reasonably required to carry out the duties to the satisfaction of the Investigators.

Holidays: 38 days per annum including public holidays and fixed days of closure.

Pension: Appointee eligible to join the USS [University Superannuation Scheme]

Duration: 2 years.

Maternity Leave: Details available upon request.

Childcare: Details available upon request.
Your appointment will be subject to:

- the satisfactory completion of a 9 month probationary period, during which the notice period will be one month on either side. Once the appointment has been confirmed, the notice period will be three months either side.
- the return of a completed medical questionnaire, and if necessary, confirmation from the University’s Occupational Health Service that you are medically fit for the post concerned (allowing for any reasonable adjustments that may be required)
- the provision of original documentation to establish your right to work and remain in the UK, which the University requires in order to comply with its duties under the Immigration, Asylum and Nationality Act 2006. It will remain your responsibility to ensure that you are able to produce such documentation as and when requested from you

Applicants who would need a work visa if appointed are asked to note that under the UK’s new points-based migration system they will need to demonstrate that they have sufficient points, and in particular that:

(i) they have sufficient English language skills (evidenced by having passed a test in basic English, or coming from a majority English-speaking country, or having taken a degree taught in English)

and

(ii) that they have sufficient funds to maintain themselves and any dependents until they receive their first salary payment.

Further information is available at: http://www.ukba.homeoffice.gov.uk/workingintheuk/tier2/generalarrangements/eligibility/

7. Applications

Applications should include:
- Curriculum Vitae;
- Covering letter describing suitability for the position and how the candidate satisfies the selection criteria;
- List of publications;
- Names, email and postal addresses of two referees (candidates should ask their referees to send their references directly to the Administrative Assistant, Mathematical Institute, 24-29 St Giles, Oxford, OX1 3LB so that they arrive before the closing date. Fax +44 (0) 1865 273583 or email vacancies@maths.ox.ac.uk is sufficient).

Please quote reference: BK/08/064

Applications should be sent to: The Administrative Assistant, Mathematical Institute, 24-29 St Giles, Oxford, OX1 3LB. Email applications (vacancies@maths.ox.ac.uk) are acceptable. The closing date for applications is lunchtime on Friday 9th January 2009. Interviews will be held in late January/early February.
Equal opportunities at the University of Oxford

As an Equal Opportunity employer, we positively encourage applications from people of different backgrounds. All our jobs are filled in line with our equal opportunities code of practice, which helps us make sure that men and women, people of different religions or beliefs, ages, racial groups, and those with disabilities are all treated fairly.

POLICY STATEMENT

The policy and practice of the University of Oxford require that all staff are afforded equal opportunities within employment. Entry into employment with the University and progression within employment will be determined only by personal merit and the application of criteria which are related to the duties of each particular post and the relevant salary structure. In all cases, ability to perform the job will be the primary consideration. Subject to statutory provisions, no applicant or member of staff will be treated less favourably than another because of his or her gender, marital or civil partnership status, sexual orientation, religion or belief, racial group, age or disability. If you have any questions about equal opportunities at the University of Oxford, please visit our web-site at www.admin.ox.ac.uk/eop.

Data protection

All data supplied by applicants will be used only for the purposes of determining their suitability for the post¹, and will be held in accordance with the principles of the Data Protection Act 1998 and the University's Data Protection Policy.

¹ But NB if the person appointed to the post is a migrant sponsored under the UK’s new points-based migration system, we are required to retain all applications for the duration of the sponsorship.